Best Practice Policy Statement on

Urologic Surgery Antimicrobial Prophylaxis

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ABSTRACT

Purpose: Antimicrobial prophylaxis is the periprocedural systemic administration of an antimicrobial agent intended to reduce the risk of postprocedural local and systemic infections. The American Urological Association (AUA) convened a Best Practice Policy Panel to formulate recommendations on the use of antimicrobial prophylaxis during urologic surgery.

Methods: Recommendations are based on a review of the literature and the Panel members' expert opinions.

Results: The potential benefit of antimicrobial prophylaxis is determined by patient factors, procedure factors, and the potential morbidity of infection. Antimicrobial prophylaxis is recommended only when the potential benefit outweighs the risks and anticipated costs (including expense of agent and administration, risk of allergic reactions or other adverse effects, and induction of bacterial resistance). The prophylactic agent should be effective against organisms characteristic of the operative site. Cost, convenience, and safety of the agent also should be considered. The duration of antimicrobial prophylaxis should extend throughout the period when bacterial invasion is facilitated and/or likely to establish an infection. Prophylaxis should begin within 60 minutes of the surgical incision (120 minutes for intravenous fluoroquinolines and vancomycin) and generally should be discontinued within 24 hours. The American Heart Association no longer recommends antimicrobial prophylaxis for genitourinary surgery solely to prevent infectious endocarditis. Justifications and recommendations for specific antimicrobial prophylactic regimens for specific categories of urologic procedures are provided.

Conclusions: The recommendations provided in this document, including specific indications and agents enumerated in the Tables, can assist urologists in the appropriate use of periprocedural antimicrobial prophylaxis.

INTRODUCTION

Surgical site infections (SSIs) and postoperative urinary tract infections (UTIs) are a common cause of patient morbidity. Surgical site infections complicate up to 5% of clean extraabdominal operations and up to 20% of intraabdominal procedures.[1] Urinary tract infections are the most common type of nosocomial infection[2], and are frequently postoperative in nature. Surgical site infections almost double the direct costs of hospitalization, and patients with SSI are more likely to be readmitted, require stay in the intensive care unit, and suffer mortality.[3]

Although the effectiveness of perisurgical antimicrobial prophylaxis in reducing SSIs and postoperative UTIs is well established, surveys have demonstrated wide variation in utilization of periprocedural antimicrobial prophylaxis, including inappropriate selection of agents, improper timing of administration, and excessive duration of prophylaxis.[4] Nationwide efforts are now underway to improve patient safety and reduce cost by standardizing antimicrobial prophylaxis and encouraging proper application. To this end, the American Urological Association (AUA) convened the Urologic Surgery Antimicrobial Prophylaxis Best Practice Policy Panel, comprised of six urologists (Appendix 1), to formulate recommendations for the use of antimicrobial prophylaxis during urologic surgery.

METHODS

Assessment of the literature by the AUA Practice Guidelines Committee suggested that insufficient information was available to derive a guideline statement on antimicrobial prophylaxis during urologic surgery based solely on literature meta-analyses. As such, the Panel was charged with developing a Best Practice Policy Statement, which uses published data in concert with expert opinion, but does not employ formal meta-analysis of the literature. A

Medline search was performed using the MeSH index headings "antimicrobial prophylaxis," "postoperative complications," "surgical wound infection," "anti-bacterial agents," and the names of specific urologic procedures, from 1996 through 2006. This initial search was supplemented by scrutiny of bibliographies and additional focused searches, and 169 publications were selected for analysis by the Panel members. These included guidelines and policies from other groups, some of which were identified by Panel members outside of the Medline search; the guidelines from other groups were considered in the Panel's deliberations. The Panel formulated recommendations based on review of all material and the Panel members' expert opinions. Levels of evidence were assigned (Appendix 2).[5] Not all references used in creation of the Panel's recommendations are cited.

This document was submitted for peer review, and comments from all 20 responding physicians and researchers were considered by the Panel in making revisions. The final document was submitted to the AUA Practice Guideline Committee and Board of Directors for approval.

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PRINCIPLES OF SURGICAL ANTIMICROBIAL PROPHYLAXIS

1. Surgical antimicrobial prophylaxis is the periprocedural systemic administration of an antimicrobial agent intended to reduce the risk of postprocedural local and systemic infections.

Antimicrobial prophylaxis is only one of several measures thought to reduce SSI. Others include bowel preparation, preoperative hair removal, antiseptic bathing, hand-washing protocol, double gloving, and sterile preparation of the operative field.

Commonly practiced, the use of mechanical bowel preparation (MBP) prior to colorectal surgery has recently been called into question. A meta-analysis of randomized clinical trials (RCTs) comparing MBP to no MBP before elective colorectal surgery found no evidence to support the use of MBP in patients undergoing elective colorectal surgery.[6] By extrapolation, the utility of MBP in urologic surgery involving the intestine also must be questioned.

Similarly, the traditional preoperative removal of hair in preparation for surgery may not be necessary. An analysis of RCTs comparing hair removal with no hair removal, different methods of hair removal, hair removal conducted at different times prior to surgery, and hair removal carried out in different settings concluded that there was no difference in SSIs among patients who had their hair removed prior to surgery and those who did not.[7] If it is desirable to remove hair, clipping and depilatory creams resulted in fewer SSIs than shaving using a razor. Finally, there was no difference in SSIs among patients shaved or clipped on the day before surgery versus the day of surgery.

A review of six RCTs involving a total of 10,007 patients undergoing surgery compared the effects of preoperative bathing with antiseptic preparation to showering with nonantiseptic preparations. The antiseptic preparation provided no benefit in terms of reducing the risk of SSI.[8]

Surgical hand scrubbing has long been considered an important aspect of surgical technique. Recently, surgical hand rubbing with an aqueous alcohol solution has been proposed as an alternative to the traditional surgical hand scrubbing. In a large RCT incorporating 4,387

patients, the two solutions were found to be comparable in regard to SSIs.[9] Compliance with hygiene guidelines was better with hand rubbing than hand scrubbing (44% versus 28%).

While double gloving protects the surgical team from contamination by reducing perforations to the innermost glove, there is no direct evidence that additional glove protection worn by the surgical team reduces surgical infection in the patient.[10]

Sterile preparation of the operative site is the cornerstone of sterile surgical technique. Many substances are effective, including ethyl alcohol, isopropyl alcohol, aqueous iodine topical solution, iodine tincture, povidone-iodine, and chlorhexidine gluconate. Recent studies call into question the skin scrub that traditionally has been performed prior to paint with a sterile substance. In a RCT of skin preparation for abdominal surgery, Ellenhorn and colleagues[11] found that scrub with povidine-iodine soap followed by paint with providine-iodine was associated with no fewer SSIs than painting with povidine-iodine alone. The combination formulation of povidone-iodine and alcohol is similar or superior to a povidone-iodine aqueous solution in terms of reducing the occurrence of SSIs[12,13], and delivers effective antimicrobial activity with only a 30-second application.[14]

Transrectal ultrasound guided prostate biopsy, performed through a grossly contaminated field, presents additional infectious considerations. There is wide variation in the topical preparation of the rectum. Otrock et al[15] found no benefit of preprocedure povidine-iodine enemas. Carey and Korman[16] concluded that sodium biphosphate enemas added no additional protection from infectious complications. Jeon and associates[17] however, found that bisacodyl suppository rectal preparation the night before or morning of the procedure did decrease infectious complications. No standard for topical preparation of the rectum prior to transrectal ultrasound guided prostate biopsy has been established.

In addition to proper sterile technique, experience suggests that other aspects of surgical technique play an important role in preventing SSIs. Gentle tissue handling, maintaining vascularity, avoiding hematomas or other unperfused spaces, and minimizing operative time are all thought to reduce the incidence of SSIs. Thus, antimicrobial prophylaxis is only one of many factors associated with a reduction in SSI, albeit a very important one.

2. The potential benefit of surgical antimicrobial prophylaxis is determined by three considerations: patient-related factors (ability of the host to respond to bacterial invasion), procedural factors (likelihood of bacterial invasion at the operative site), and the potential morbidity of infection.

The ability of the host to respond to bacteriuria or bacteremia is affected by the specific patient-related factors described in Table 1.[18] The first six factors increase the risk of infection by impairing the natural defense mechanisms of the urinary tract and immune system. The last four factors increase the local bacterial concentration and/or the spectrum of the bacterial flora. Infections are more likely to occur because of increased inocula or are more difficult to treat because of increased bacterial resistance, respectively. These factors frequently act in an additive manner, compounding their impact. Moreover, the effect of some conditions is difficult to specify. For example, a patient with well-controlled diabetes mellitus has little impairment of bacterial immunity, whereas the poorly controlled diabetic may be clinically immunodeficient. The clinician should use judgment as to the influence of these various factors as no absolute values can be used to determine their precise effect on the patient's immunological response.

The likelihood of bacterial invasion is also affected by the amount of bacteria at the site of the surgical procedure as classified in Table 2.[19] Of note, all procedures entering the urinary

tract are considered "clean-contaminated." The likelihood of bacterial invasion is increased if bacteriuria is present or good wound preparation and surgical technique, are not applied.

The third type of factor in determining the potential benefit of prophylaxis is the potential morbidity of infection. For example, an episode of cystitis which has little risk in a healthy person can cause serious complications in a recently immunosuppressed patient after organ transplantation. Similarly, potential seeding of a prosthetic joint enhances the sequelae of systemic infections.

A thorough understanding of the impact of these factors and careful assessment of the situation of each patient is required to direct antimicrobial prophylaxis for a urologic procedure.

3. Surgical antimicrobial prophylaxis is recommended only when the potential benefit exceeds the risks and anticipated costs.

Data regarding the costs associated with prophylactic antimicrobial use specifically for urologic surgery are not readily obtainable, but data from other surgical disciplines are enlightening. Clearly, SSIs are associated with poorer patient outcome and increased costs.[20] Herwaldt and associates[21] reviewed the outcomes of 3,864 surgical patients (general, cardiothoracic, and neurosurgical) with an overall nosocomial infection rate of 11.3%. Even after accounting for covariates, nosocomial infection was associated with increased postoperative length of stay, hospital readmission rate, and outpatient use of antimicrobial agents - all of which significantly increased costs and utilization of medical resources. A recent large review of data from European centers confirmed the great cost of SSIs.[22] Moreover, it has also been demonstrated in a variety of settings that surgical antimicrobial prophylaxis, by reducing the incidence of SSIs, reduces costs.[23-26] Conversely, excess and/or inappropriate antimicrobial

prophylaxis increase costs, which is reversed by measures to improve compliance with evidence-based recommendations.[27]

Prophylactic antimicrobial use is associated with financial, personal-health, and public-health costs. Included in the consideration of the financial impact are the expense of the agent, route of administration, associated administration supplies, and labor. Costs vary widely with the antimicrobial agent selected and also according to the setting in which the administration occurs. Another important factor is variation in the duration of antimicrobial prophylaxis. A single preoperative administration has less total associated cost than a cycle of three administrations during the 24-hour perioperative period. Finally, the ultimate financial cost of antimicrobial prophylaxis incorporates both the costs associated with the agent and the costs associated with patient outcomes (SSIs, adverse reactions, etc.). Comprehensive cost differences between different regimens can be demonstrated.[28-30]

The personal-health risks of prophylactic antimicrobial administration include allergic reactions, which vary from minor rashes to anaphylaxis, and suppression of normal bacterial flora, which can lead to *Clostridium difficile* colitis, colonization and infection with resistant organisms, and other adverse effects. Although the frequency of adverse events for any specific antimicrobial agent is calculable for population exposures, it is difficult to assess the gravity of each adverse event, as well as the need for specific interventions to treat consequences of the adverse events. Nevertheless, all of these factors are components of the financial impact of prophylactic antimicrobial use. In general, the financial costs of prophylaxis are controlled by using the least expensive and safest efficacious agent for the shortest duration that is consistent with good clinical practice.

The public-health risk of antimicrobial prophylaxis relates to the induction of bacterial resistance in the patient and in the community microbial reservoir. Antimicrobial usage has had a clear impact on the emergence of resistant bacterial strains.[31] A substantial cause of the emergence of these resistant strains is the over-use (treatment when none is needed and prolonged therapy exposures) of antimicrobial agents for all indications. Data suggesting that fluoroquinolone resistance is rising in areas of high use support the contention that microbial resistance is directly related to repetitive exposure of microbes to unique antimicrobial agents.[32] It is likely that the appropriate use of antimicrobial prophylaxis (indication-specific and of limited duration) would limit these resistance trends.

4. The antimicrobial agent used for prophylaxis should be effective against the disease-relevant bacterial flora characteristic of the operative site. Cost, convenience, and safety of the agent also should be considered.

The choice of the appropriate antimicrobial agent to be used for prophylaxis takes into account both the surgical site and the properties of the antimicrobial agent. The agent should achieve serum and tissue levels of drug that exceed the minimum inhibitory concentration for organisms characteristic of the operative site. Furthermore, the optimal agent should have a long half-life so as to maintain sufficient serum and tissue concentrations for the duration of the procedure without the need for redosing. The agent should be safe, inexpensive, and not likely to promote bacterial resistance.

For the urinary tract, the cephalosporins, fluoroquinolones, and aminoglycosides are generally efficacious, have a long half-life, are inexpensive (when used as single dose) and are rarely associated with allergic reactions. Furthermore, the latter two classes of antimicrobials can

be used in patients with a beta-lactam allergy. While the incidence of adverse reaction to cephalosporins in patients with a penicillin allergy is low, consideration of an alternative agent is recommended in cases of significant penicillin allergy.

A number of antimicrobial agents may effectively cover the expected organisms and satisfy the criteria outlined above. Optimally, the specific prophylactic regimen should be supported by clinical trials. In many cases, RCTs are not available; such lack of data does not preclude the appropriateness of some regimens based upon drug efficacy, cost, safety, and knowledge of the surgical site flora. When selecting the agent for antimicrobial prophylaxis, the clinician must be cognizant of varying resistance patterns in the local community. Specifically, fluoroquinolone resistance, which is increasing in prevalence,[33] must be considered given the high utilization of these agents for urologic surgery antimicrobial prophylaxis.

5. The duration of surgical antimicrobial prophylaxis should extend throughout the period in which bacterial invasion is facilitated and/or is likely to establish an infection.

For prophylactic antimicrobial administration to be optimally effective, timing and dosing are critical. Infusion of the first dose should begin within 60 minutes of the surgical incision (with the exception of 120 minutes for intravenous fluoroquinolones and vancomycin). As with timing, correct dosing is equally important. Some drugs should be adjusted to the patient's body weight (or corrected dosing weight) or body mass index. Additional doses are required intraoperatively if the procedure extends beyond two half-lives of the initial dose.[1]

With few exceptions, the published literature suggests that antimicrobial prophylaxis is unnecessary after wound closure or upon termination of an endoscopic procedure.[1, 19] Thus, in most cases, antimicrobial prophylaxis should be a single dose, or at least discontinued within 24

hours of the end of the procedure. Misuse of antimicrobials is associated with bacterial resistance, morbidity, and increased health care costs.[34] Three circumstances in which a longer duration of antimicrobials are frequently considered include the placement of prosthetic material, the presence of an existing infection, and the manipulation of an indwelling tube.

The literature offers little guidance on the duration of antimicrobial therapy after prosthesis (e.g., penile implant) placement. While theoretical concerns of biofilm development may prompt the use of a longer course of antimicrobials, this practice is not well supported in the literature. Indeed, data from the joint replacement literature indicate that prophylaxis should be discontinued within 24 hours of the procedure.[1] Furthermore, the impregnation of implantable penile prostheses with antimicrobials appears to reduce the incidence of prosthetic infections and should further reduce the temptation to overuse systemic antimicrobials in this situation.[35,36]

In cases where an existing infection is present (e.g., bacteriuria at the time of endoscopic procedure, devitalized tissue, colonized stone, etc.), a therapeutic course of antimicrobials should be administered in an attempt to sterilize the field. In some cases, such as the treatment of a patient with an indwelling urinary catheter or an infected urinary stone, the coexisting infection cannot be eradicated prior to the procedure. In such instances, the aim of preoperative antimicrobial therapy is to suppress the bacterial count prior to surgery. The subsequent course of antimicrobials, which is therapeutic rather than prophylactic, might include a period extending beyond 24 hours from the conclusion of the procedure depending on patient-risk factors and the implications of infection-related morbidity for the patient. When possible, coexisting infections should be treated prior to the procedure to reduce SSIs.

In the absence of preexisting bacterial colonization, there is no evidence that prophylaxis should extend beyond 24 hours following a procedure. In cases where prolonged catheterization

follows the procedure (e.g., radical prostatectomy), antimicrobial therapy at the time of catheter removal may be therapeutic rather than prophylactic, since colonization has likely occurred. One option is to culture the urine 24 to 48 hours prior to intended catheter removal, and administer culture-directed therapy. This is not practical in many cases of catheterization for only 48 to 72 hours, and may be misleading. The other option is to administer antimicrobial treatment empirically. The Panel does not make a recommendation as to which option is preferable. The duration of therapeutic treatment in such cases is unclear and likely depends on host factors, the duration of catheterization, and the potential morbidity of infection. There is no evidence that additional antimicrobials should be used when nonurinary tract external drains are removed.

ANTIMICROBIAL PROPHYLAXIS RECOMMENDATIONS

An important change in antimicrobial prophylaxis pertaining to urologists is that antimicrobials are no longer recommended by the American Heart Association in association with genitourinary procedures solely to prevent infectious endocarditis.[37] Although infectious endocarditis remains a life-threatening disease, with some cardiac conditions predisposing to infectious endocarditis and bacteremia with organisms causing infectious endocarditis occurring commonly in association with genitourinary procedures, the American Heart Association now recommends that antimicrobial prophylaxis during genitourinary procedures is not an effective strategy for prevention of infectious endocarditis. Infectious endocarditis is more likely to result from random bacteremias associated with daily activities than from those caused by genitourinary procedures. Prophylaxis may prevent only a very small number of cases of infectious endocarditis, if any, in individuals undergoing genitourinary procedures. Overall, the risk of antimicrobial-associated adverse events exceeds the benefit from prophylactic

antimicrobial therapy solely to prevent infectious endocarditis in patients undergoing genitourinary procedures.

The use of oral fluoroquinolines as a prophylactic agent in urologic endoscopic surgery is a special situation. This antimicrobial regimen is rarely used for prophylaxis outside of urologic surgery. Level Ib evidence supporting this practice is found in four RCTs comparing oral ciprofloxacin to intravenous cephalosporins, which involved a total of 345 patients undergoing a variety of endoscopic urologic procedures, including ureteral stent placement, ureteroscopy, retrograde pyelography, bladder biopsy, urethrotomy, collagen injection, transurethral resection of prostate, transurethral resection of bladder tumor, cystolithalopaxy, and transurethral incision of bladder neck contracture.[38-41] In all four studies the incidence of postoperative bacteriuria was not different between the two groups, and costs were lower in the ciprofloxacin groups owing to the simpler use of oral rather than intravenous administration. Other studies have confirmed the effectiveness of oral fluoroquinolines for urological surgery antimicrobial prophylaxis in a number of settings.[16,42-51]

The Panels' recommendations are provided in Tables 3 and 4[52], and levels of evidence with justifications are provided in the text below. Recommended Antimicrobial Prophylaxis for Urologic Procedures, Table 3a, lists those procedures for which antimicrobial prophylaxis is recommended, as well as the agent(s) of choice, alternative agents, and duration of therapy. Important considerations are the limitation of prophylaxis to patients with risk factors in some cases and the recommendation that prophylaxis should not exceed 24 hours. In cases where an external urinary catheter is present prior to or is placed at the time of the procedure, additional antimicrobial treatment (≤24 hours) is recommended in patients with risk factors. Alternatively, a full course of culture-directed antimicrobial can be administered for documented bacteriuria, or

treatment can be omitted if the urine culture shows no growth. Antimicrobials and Dosages, Table 3b, lists the recommended doses and dosing intervals for the agents listed in Table 3a. For some procedures, dosing may need to be more frequent than the intervals listed in Table 3b. Table 4 provides recommendations for Antimicrobial Prophylaxis for Patients with Orthopedic Considerations.[52] In all cases, the absence of an agent in the Tables does not preclude its appropriate use, depending on specific situations – including medication intolerance, agent compatibility, prior infection history of the patient, and community resistance patterns. The Panel's recommendations are generally similar, but differ in varying specific situations, to guidelines from other groups and recognized references.[53-58]

Removal of external urinary catheter (prophylaxis indicated if risk factors)

Level of evidence: Ib, III, IV

Options for treatment of a patient at the time of removal of an external urinary catheter include empiric therapy with agents indicated in Table 3a, or culture-directed antimicrobials. Treatment is not necessary if the urine is documented to show no growth. Additionally, prophylactic antimicrobials have not been demonstrated to be beneficial in patients undergoing clean intermittent catheterization[59] or long-term catheterization.[60] The rate of bacteriuria in short-term catheterized patients is 5% to 10% for each day the catheter is in place.[61-63] Given that noninfectious urinary tract disease is a risk factor for developing bacteremia in the presence of bacteriuria[64], antimicrobial treatment at the time of catheter removal following urinary tract surgery may be warranted. In two RCTs involving 146 patients after transurethral surgery it was found that patients receiving cefotaxime at the time of catheter removal (single dose in one study, three-day course in the other), compared to a control group not receiving antimicrobials at catheter removal,

had significantly reduced postoperative complication rate and hospital stay.[65,66] In the nonurologic setting, Harding and associates[67] performed a RCT comparing oral antimicrobials with no treatment in women with catheter-acquired bacteriuria after short-term catheter use. Bacteriuria resolved without treatment in 36%, but oral antimicrobial use significantly increased the elimination of bacteriuria, to 81%. Of the untreated patients with asymptomatic bacteriuria, 17% developed symptoms. An analysis in the Cochrane Database of Systematic Reviews concluded that there is limited evidence indicating that receiving antimicrobials during the first three postoperative days, or from postoperative day two until catheter removal, reduces the rate of bacteriuria and other signs of infection in surgical patients with bladder drainage for at least 24 hours postoperatively.[68] The Panel concludes that the benefits for antimicrobial prophylaxis at removal of an external urinary catheter most likely accrue to patients with risk factors (Table 1). Alternatively, a full course of culture-directed antimicrobial can be administered for documented bacteriuria, or treatment can be omitted if the urine culture shows no growth.

Cystography, urodynamic study, or simple cystourethroscopy (prophylaxis indicated if risk factors)

Level of evidence: Ib, III, IV

Antimicrobial prophylaxis for cystography, urodynamic study, or simple cystourethroscopy is probably not necessary if the urine culture shows no growth. For the outpatient diagnostic procedures, however, such documentation is often lacking. A negative urinalysis is reassuring, but does not preclude the possibility of postprocedure urinary tract infection. A decision-analysis model based upon estimates from the literature and consensus suggested that prophylactic antimicrobials after urodynamic studies are beneficial once the rate

of urinary tract infection without antimicrobials exceeds 10%.[69] Conversely, a RCT involving a single oral dose of ciprofloxacin versus placebo in 192 patients who had urine without growth before urodynamic study found that postprocedure urinary tract infections decreased significantly, from 14% to 1%, with prophylaxis; the authors recommended antimicrobial prophylaxis for all patients undergoing urodynamic study.[51] With regards to cystourethroscopy, Rané and associates[70] performed a RCT comparing a single dose of parenteral gentamicin with placebo in 162 patients, and found that prophylaxis significantly reduced the rate of postcystourethroscopy positive urinalyses from 21% to 5%. More recently Johnson and colleagues[71] reported a RCT completed by 2083 patients receiving placebo, 200 mg trimethoprim orally, or 500 mg ciprofloxacin orally. The rate of bacteriuria five days later was significantly reduced by treatment, at 9%, 5%, and 3%, respectively. Since there are, however, some RCTs that demonstrate no reduction by prophylaxis of infection rates associated with cystography[72], urodynamic study[73,74], or cystourethroscopy[75], the Panel concludes that antimicrobial prophylaxis is justified in this setting only in patients with risk factors (Table 1).[18]

Cystourethroscopy with manipulation (prophylaxis indicated in all patients)

Level of evidence: Ia/b, IV

The most convincing evidence supporting the use of antimicrobial prophylaxis for this category of procedures is in association with transurethral resection of the prostate. Berry and Barratt[76] performed a meta-analysis of 32 RCTs comprising 4,260 patients, and confirmed that antimicrobial prophylaxis prior to transurethral resection of the prostate significantly reduced both the incidence of both bacteriuria (26% to 9.1%) and clinical sepsis(4.4% to 0.7%). Clinical efficacy was proven for a number of antimicrobial classes, including fluoroquinolones,

cephalosporins, aminoglycosides, and trimethoprim-sulfamethoxazole. A subsequent meta-analysis using updated methodology came to the same conclusion.[77] A recent RCT of 400 patients undergoing transurethral resection of the prostate, comparing a single dose of levofloxacin, a single dose of trimethoprim-sulfamethoxazole, and no antimicrobials, revealed a significantly greater overall use of antimicrobials in the control group; the two antimicrobial regimens were similar in efficacy.[49] In a RCT of 243 patients undergoing transurethral resection of bladder tumor, three perioperative doses of cephradine, compared to no antimicrobial, reduced the rate of bacteriuria significantly.[78] Similar RCTs have not been performed for other cystoscopic procedures involving transurethral manipulation (bladder biopsy, ureteral catheterization, laser prostatectomy, etc.), but the similarities of these other cystoscopic procedures in terms of invasiveness and potential tissue trauma suggest that the data regarding transurethral resection of the prostate and bladder tumor reasonably can be extrapolated to other cystoscopic procedures with manipulation.

Prostate brachytherapy or cryotherapy (need for prophylaxis uncertain)

Level of evidence: III, IV

There are no RCTs regarding the use of antimicrobial prophylaxis for prostate brachytherapy or cryotherapy. Nonetheless, antimicrobial prophylaxis is routinely used. One group reported that only one in 125 patients undergoing transperineal prostate brachytherapy suffered a symptomatic urinary tract infection with the use of a single perioperative intravenous dose of cefazolin[79], but in another study there was only a 2% incidence of postimplant febrile episodes without the use of antimicrobial prophylaxis (nonfebrile urinary tract infections were not considered).[80] Among 517 patients undergoing prostate brachytherapy of whom 258 received

perioperative antimicrobials, the incidence of epididymitis was 0.4% in the patients who received perioperative antimicrobials compared to 1.5% in the group without antimicrobials.[81] There are no data available regarding prostate cryotherapy and antimicrobial prophylaxis. The destructive nature of the treatments coupled with entry near a clean-contaminated space makes the use of antimicrobial prophylaxis by many practitioners a reasonable consideration, but the Panel cannot provide a specific recommendation.

Transrectal prostate biopsy (prophylaxis indicated in all patients)

Level of evidence: Ib

A large RCT of 537 patients receiving oral ciprofloxacin or placebo before transrectal needle biopsy of the prostate revealed the incidence of bacteriuria to be significantly lower in the antimicrobial group.[44] In a three-armed RCT (231 patients) comparing placebo, a single dose of ciprofloxacin and tinidazole, and the same combination twice a day for three days, the incidence of all infectious complications, and specifically urinary tract infection was significantly lower in both antimicrobial groups. Moreover, the single dose was as effective as the three-day dosing.[45] Additional RCTs confirm the equivalence of single-dose or one-day regimens compared to three-day regimens.[48,50]

Shock-wave lithotripsy (prophylaxis indicated in all patients)

Level of evidence: Ia

A meta-analysis of eight RCTs assessing the efficacy of antimicrobial prophylaxis for shock-wave lithotripsy demonstrated a benefit of therapy in significantly reducing the incidence of postoperative bacteriuria from a median of 5.7% to 2.1%, even with preoperative urine

showing no growth. Subgroup analysis to assess the effectiveness of a particular regimen could not be performed due to the wide variability in practice patterns.[82]

Percutaneous renal surgery (prophylaxis indicated in all patients)

Level of evidence: IIb, III

There are no RCTs that confirm the need for antimicrobial prophylaxis for percutaneous renal surgery. Nonetheless, an enlightening report from 1986 suggests that antimicrobial prophylaxis likely will reduce significantly infectious complications. Charton and associates[83] performed percutaneous nephrolithotomy in 107 patients with preoperative urine showing no growth, without antimicrobial prophylaxis. Of the patients, 35% suffered a postoperative urinary tract infection. In comparison, a prospective but nonrandomized assessment of 49 patients undergoing percutaneous nephrostolithotomy and receiving oral ciprofloxacin, intravenous ciprofloxacin, or no antimicrobial treatment found postoperative urinary tract infection to occur in 17%, 0%, and 40% of patients, respectively.[42] With regards to duration of prophylaxis, one prospective comparative study found that single-dose therapy with ofloxacin was associated with the same incidence of fever, bacteriuria, and bacteremia as ofloxacin administered until the time of nephrostomy tube removal.[47]

Ureteroscopy (prophylaxis indicated in all patients)

Level of evidence: Ib

In a RCT involving 113 patients undergoing ureteroscopy for stone removal, randomized to a single oral dose of levofloxacin versus no antimicrobials, the treatment arm had a

significantly lower incidence of postoperative bacteriuria (13% versus 2%).[84] Another author suggests that the expected rate of bacteriuria after ureteroscopy without prophylaxis might be in excess of 30%, with an expected rate of febrile urinary tract infection of 4% to 25%.[56] Prophylaxis with oral ciprofloxacin was similar to intravenous cefazolin in terms of the incidence of urinary tract infection and sepsis in another RCT of 77 patients undergoing endourologic surgery, of whom 42 underwent ureteroscopy or ureteral stent placement.[41]

Vaginal surgery (prophylaxis indicated in all patients)

Level of evidence: Ia/b, IIb

In one prospective study of urethropexy, comparing intravenous cefazolin in 14 women to no antimicrobials in 12 women, postoperative fever and hospital stay were significantly less in patients who received prophylactic antimicrobials.[85] Randomized controlled trials involving antimicrobial prophylaxis for vaginal urologic surgery have not been reported, but considerable evidence exists regarding vaginal hysterectomy, which can be considered similar to vaginal urologic surgery in terms of infection risk. Duff and Park[86] found in their meta-analysis of antimicrobial prophylaxis for vaginal hysterectomy that, without exception, studies demonstrated a dramatic decrease in the incidence of pelvic infections when antimicrobial prophylaxis was used. Regarding duration of therapy, one RCT of patients undergoing vaginal hysterectomy determined that a course of antimicrobials less than 24 hours was as effective as a long course in preventing postoperative infections.[87]

Open or laparoscopic surgery without entering urinary tract (prophylaxis indicated if risk factors)

Level of evidence: Ib, III, IV

This category includes a number of transabdominal, retroperitoneal, cutaneous, and genital procedures. Results in a group of 83 patients undergoing transabdominal radical nephrectomy randomized to a single dose of intravenous cephalosporin versus no perioperative prophylaxis revealed a significantly lower overall infection rate in the treatment group (8% versus 27%).[88] In a prospective but nonrandomized comparison of 424 hand-assisted laparoscopic nephrectomies with and without antimicrobial prophylaxis (cephalosporin), wound infections occurred significantly more often in patients without prophylaxis (13% versus 5.4%).[89] As there are limited data for other urologic procedures in this category, the Panel's recommendation is tempered by meta-analyses evaluating antimicrobial prophylaxis for nonurologic "clean" abdominal surgery that provide mixed support for antimicrobial prophylaxis in this setting.[90-93]

Open or laparoscopic surgery involving entry into urinary tract (prophylaxis indicated in all patients)

Level of evidence: Ib, III, IV

One comprehensive review of the literature regarding surgery with entry into the urinary tract concluded that the expected rate of febrile urinary tract infection is 5% to 10% without prophylaxis, and that antimicrobial prophylaxis likely would reduce significantly the rate of febrile urinary tract infection, to 2% to 3%.[56] In a RCT of 91 men undergoing open prostatectomy, intravenous cefotaxime (compared to no prophylaxis) significantly reduced the incidence of postoperative infection from 46% to 5%.[94] Regarding duration of prophylaxis, one

RCT confirmed that one day of intravenous cephalosporin was equivalent to four days of the same agent for preventing postoperative infections after radical prostatectomy.[95]

Open or laparoscopic surgery involving intestine (prophylaxis indicated in all patients)

Level of evidence: Ia, IV

Although RCTs involving urologic surgery involving bowel (primarily urinary diversion, with or without cystectomy) have not been reported, meta-analyses of percutaneous endoscopic gastrostomy[96], appendectomy[97], and colorectal surgery [98] confirm benefit to antimicrobial prophylaxis in the setting of surgery involving intestinal components.

Open or laparoscopic surgery involving implanted prosthesis (prophylaxis indicated in all patients)

Level of evidence: Ia, IV

The implantation of foreign material raises the specter of disastrous infectious complications. Although there are no RCTs regarding antimicrobial prophylaxis for insertion of penile prostheses, meta-analyses of mesh hernia repair [99] and orthopedic surgery [100] confirm that antimicrobial prophylaxis is beneficial when foreign material is implanted. A prolonged course of antimicrobials has been used by many practitioners following penile prosthesis insertion, but evidence from the orthopedic literature suggests that prophylaxis for 24 hours or less is adequate.[1]

SUMMARY

Surgical site infections and UTIs are major sources of postoperative morbidity. Antimicrobial prophylaxis is an important preventative measure, and is an easily modifiable

component of a program to reduce postoperative infections. The decision to use antimicrobial prophylaxis in urological surgery, and the selection of agent and dosing, can start with guidelines such as the ones presented in this document. The appropriate use of antimicrobial prophylaxis in an individual patient, however, requires consideration of not only these guidelines but also a comprehensive evaluation of the patient's specific circumstances.

TABLES

Table 1: Patient-related factors affecting host response to surgical infections

Advanced age
Anatomic anomalies of the urinary tract
Poor nutritional status
Smoking
Chronic corticosteroid use
Immunodeficiency
Externalized catheters
Colonized endogenous/exogenous material
Distant coexistent infection
Prolonged hospitalization

Modified from reference.[18]

Table 2: Surgical wound classification

Clean	Uninfected operative site, with primary skin closure.
Clean-contaminated	Entry into respiratory, alimentary, genital, or urinary tracts.
Contaminated	Fresh accidental wounds, major break in sterile technique, gross spillage from gastrointestinal tract, or presence of acute but nonpurulent inflammation at the operative site.
Dirty-infected	Old accidental wound with devitalized tissue or presence of clinical infection or perforated viscera at the operative site. This definition implies that organisms that might cause postoperative infection were present at the operative site before surgery.

Adapted from reference.[19]

Table 3a. Recommended antimicrobial prophylaxis for urologic procedures

Procedure	Organisms	Prophylaxis Indicated	Antimicrobial(s) of Choice	Alternative Antimicrobial(s)	Duration of Therapy*
Lower Tract Instrumentation					
Removal of external urinary catheter	GU tract†	If risk factors‡,§	- Fluoroquinolone¶ - TMP-SMX¶	- Aminoglycoside ± Ampicillin¶ - 1st/2nd gen. Cephalosporin¶ - Amoxacillin/Clavulanate¶	≤24 hours¶
Cystography, urodynamic study, or simple cystourethroscopy	GU tract	If risk factors§	- Fluoroquinolone - TMP-SMX	- Aminoglycoside ± Ampicillin - 1st/2nd gen. Cephalosporin - Amoxacillin/Clavulanate	≤24 hours
Cystourethroscopy with manipulation‖	GU tract	All	- Fluoroquinolone - TMP-SMX	- Aminoglycoside ± Ampicillin - 1st/2nd gen. Cephalosporin - Amoxacillin/Clavulanate	≤24 hours
Prostate brachytherapy or cryotherapy	Skin	Uncertain	- 1st gen. Cephalosporin	- Clindamycin**	≤24 hours
Transrectal prostate biopsy	Intestine††	All	- Fluoroquinolone	- Aminoglycoside + Metronidazole or Clindamycin**	≤24 hours
Upper Tract Instrumentation					
Shock-wave lithotripsy	GU tract	All	- Fluoroquinolone - TMP-SMX	- Aminoglycoside ± Ampicillin - 1st/2nd gen. Cephalosporin - Amoxacillin/Clavulanate	≤24 hours
Percutaneous renal surgery	GU tract and skin‡‡	All	- 1st/2nd gen. Cephalosporin - Aminoglycoside + Metronidazole or Clindamycin	- Ampicillin/Sulbactam - Fluoroquinolone	≤24 hours
Ureteroscopy	GU Tract	All	- Fluoroquinolone - TMP-SMX	- Aminoglycoside ± Ampicillin - 1st/2nd gen. Cephalosporin - Amoxacillin/Clavulanate	≤24 hours
Open or Laparoscopic Surgery					
Vaginal surgery	GU tract, skin and Grp B *Strep.*	All	- 1st/2nd gen. Cephalosporin - Aminoglycoside + Metronidazole or Clindamycin	- Ampicillin/Sulbactam - Fluoroquinolone	≤24 hours
Without entering urinary tract	Skin	If risk factors	- 1st gen. Cephalosporin	- Clindamycin	Single dose
Involving entry into urinary tract	GU tract and skin	All	- 1st/2nd gen. Cephalosporin - Aminoglycoside + Metronidazole or Clindamycin	- Ampicillin/Sulbactam - Fluoroquinolone	≤24 hours
Involving intestine §§	GU tract, skin and intestine	All	- 2nd/3rd gen. Cephalosporin - Aminoglycoside + Metronidazole or Clindamycin	- Ampicillin/Sulbactam - Ticarcillin/Clavulanate - Pipercillin/Tazobactam - Fluoroquinolone	≤24 hours
Involving implanted prosthesis	GU tract and skin	All	- Aminoglycoside + 1st/2nd gen. Cephalosporin or Vancomycin	- Ampicillin/Sulbactam - Ticarcillin/Clavulanate - Pipercillin/Tazobactam	≤24 hours

Order of agents in each column is not indicative of preference. The absence of an agent does not preclude its appropriate use depending on specific situations.

Key

* Additional antimicrobial therapy may be recommended at the time of removal of an externalized urinary catheter.

† GU tract: Common urinary tract organisms are *E. coli, Proteus sp., Klebsiella sp., Enterococcus.*

‡ See Table 1 "Patient-related factors affecting host response to surgical infections."

§ If urine culture shows no growth prior to the procedure, antimicrobial prophylaxis is not necessary.

¶ Or full course of culture-directed antimicrobials for documented infection (which is treatment, not prophylaxis).

‖ Includes transurethral resection of bladder tumor and prostate, and any biopsy, resection, fulguration, foreign body removal, urethral dilation or urethrotomy, or ureteral instrumentation including catheterization or stent placement/removal.

******Clindamycin, or aminoglycoside + metronidazole or clindamycin, are general alternatives to penicillins and cephalosporins in patients with penicillin allergy, even when not specifically listed.

†† Intestine: Common intestinal organisms are *E. coli, Klebsiella sp., Enterobacter, Serratia sp, Serratia sp., Proteus sp., Enterococcus*, and Anaerobes.

‡‡ Skin: Common skin organisms are *S. aureus*, coagulase negative *Staph. sp*., Group A *Strep. sp*.

§§ For surgery involving the colon, bowel preparation with oral neomycin plus either erythromycin base or metronidazole can be added to or substituted for systemic agents.

Key: gen, generation; GU, genitourinary; TMP-SMX, trimethoprim-sulfamethoxazole.

Table 3b: Antimicrobial agents and doses for periprocedure use

- For surgical prophylaxis, all agents should be administered IV except fluoroquinolones, trimethoprim-sulfamethoxazole, oral agents for bowel preparation, and some agents given at catheter removal.
- Dosages may vary with specific patient and situation.
- For prolonged procedures, repeat intraoperative dosing may be indicated sooner than the intervals indicated in the Table.
- Level-based dosing can be used for several agents, but is not applicable to periprocedural use less than or equal to 24 hours, and as such are not included in the Table.
- Drug classification lists are not all-inclusive.

Fluoroquinolones	Levafloxacin: 500 mg PO single dose Ciprofloxacin: 500 mg PO [q12h] Ofloxacin: 400 mg PO [q12h]
Aminoglycosides	Gentamicin: 5 mg/kg IV single dose Tobramycin: 5 mg/kg IV single dose Amikacin: 15 mg/kg IV single dose
1st Generation cephalosporins	Cephalexin: 500 mg PO [q6h] Cephradine: 500 mg PO [q6h] Cefadroxil: 500 mg PO [q12h] Cefazolin: 1 g IV [q8h]
2nd Generation cephalosporins	Cefaclor: 500 mg PO [q8h] Cefprozil: 500 mg PO [q12h] Cefuroxime: 500 mg PO [q12h] Cefoxitin: 1 - 2 g IV [q8h]
3rd Generation cephalosporins (oral agents not listed)	Ceftizoxime: 1 g IV [q8h] Ceftazidime: 1 g IV [q12h] Ceftriaxone: 1 - 2 IV single dose Cefotaxime: 1 g IV [q8h]
Others	Amoxicillin/clavulanate: 875 mg PO [q12h] Ampicillin: 1 - 2 g IV [q6h] Ampicillin/sulbactam: 1.5 - 3 g IV [q6h] Clindamycin: 600 mg IV [q8h] Erythromycin base (for bowel preparation): 1 - 2 g PO [variable] Metronidazole: 1 g IV [q12h]; (for bowel preparation) 1 - 2 g PO [variable] Neomycin (for bowel preparation): 1 - 2 g PO [variable] Pipercillin/tazobactam: 3.375 g IV [q6h] Ticarcillin/clavulanate: 3.1 g IV [q6h] Trimethoprim-sulfamethoxazole: 1 double-strength tablet PO [q12h] Vancomycin: 1 g IV [q12h]

Key: g, gram; h, hour; IV, intravenous; kg, kilogram; mg, milligram; PO, orally; q, every.

Table 4: Antimicrobial prophylaxis for patients with orthopedic conditions

- Antimicrobial prophylaxis is not indicated for urologic patients on the basis of orthopedic pins, plates, and screws, nor is it routinely indicated for most urologic patients with total joint replacements on that basis alone.
- Antimicrobial prophylaxis intended to reduce the risk of hematogenous total joint infection is recommended in patients who meet BOTH sets of criteria in the table below. The recommended antimicrobial regimen in these patients include:
    - A single systemic level dose of a quinolone (e.g., ciprofloxacin, 500 mg; levofloxacin, 500 mg; ofloxacin, 400 mg) orally one to two hours preoperatively.
    - Ampicillin 2 gm IV (or vancomycin 1 g IV over one to two hours in patients allergic to ampicillin) plus gentamicin 1.5 mg/kg IV 30 to 60 minutes preoperatively.
    - For some procedures, additional or alternative agents may be considered for prophylaxis against specific organisms and/or other infections.
- For patients NOT meeting BOTH of these criteria, antimicrobial prophylaxis still may be indicated to reduce the risk of other infections.

Increased risk of hematogenous total joint infection	**Increased risk of bacteremia associated with urologic procedures**
Patients during the first two years after prosthetic joint replacement Immunocompromised patients with prosthetic joint replacements • Inflammatory arthropathies (e.g., rheumatoid arthritis, systemic lupus erythematosus) • Drug-induced immunosuppression • Radiation-induced immunosuppression Patients with prosthetic joint replacements and comorbidities • Previous prosthetic joint infections • Malnourishment • Hemophilia • HIV infection • Diabetes • Malignancy	Any stone manipulation (includes shock-wave lithotripsy) Any procedure with transmural incision into urinary tract (does not include simple ligation with excision or percutaneous drainage procedure) Any endoscopic procedures of upper tract (ureter and kidney) Any procedure that includes bowel segments Transrectal prostate biopsy Any procedure with entry into the urinary tract (except for urethral catheterization) in individuals with higher risk of bacterial colonization: • Indwelling catheter or intermittent catheterization • Indwelling ureteral stent • Urinary retention • History of recent/recurrent urinary tract infection or prostatitis • Urinary diversion

Adapted from reference.[52]

Key: g, gram; IV, intravenous; kg, kilogram; mg, milligram.

Appendix 1. **Urologic Surgery Antimicrobial Prophylaxis Best Practice Policy Panel**

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Appendix 2: Levels of evidence[5]

Ia. Evidence obtained from meta-analysis of randomized trials

Ib. Evidence obtained from at least one randomized trial

IIa. Evidence obtained from at least one well-designed controlled study without randomization

IIb. Evidence obtained from at least one other type of well-designed quasi-experimental study

III. Evidence obtained from well-designed nonexperimental studies, such as comparative studies, correlation studies, and case reports

IV. Evidence obtained from expert committee reports, or opinions, or clinical experience of respected authorities

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